Universität Basel

Research Project

Global analysis of RNA processing in muscle cell-motor neuron co-cultures of spinal muscular atrophy (SMA) patients

Third-party funded project

Project title Global analysis of RNA processing in muscle cell-motor neuron co-cultures of spinal muscular atrophy (SMA) patients
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Spinal muscular atrophy (SMA) is a neuromuscular disease that results in muscle weakness due to degeneration of the interface between the motor neuron and muscle cells. In the most severe forms, SMA type 1 and 2, children at early age are affected. Tragically, in these two forms of the disease, progression is rapid and leads to a fatal outcome at the age of 2-5 years. Unfortunately, no treatment for SMA is currently available. In most cases, SMA is caused by a mutation in the SMN1 gene (survival of motor neuron 1) – the severity of the disease might be linked to different degrees of compensation of absence of SMN1 by the related SMN2 gene. Strikingly, despite knowing the mutations and the gene that cause SMA, very little is known about the physiological function of SMN and the motor neuron- and muscle-specific pathology that is caused by mutations in SMN1, which is expressed in all cells in our body. In recent years, a role for SMN in the processing of RNAs has been proposed.

In our project, we plan to use a well-defined system of muscle stem cells obtained from healthy volunteers and SMA type 2 patients that are co-cultured with motor neurons to study how the interface between muscle and nerve, the neuromuscular junction, is pathologically affected in this disease. Furthermore, we aim at establishing and using novel techniques and biocomputational analysis methods to investigate how lack of adequate SMN function affects RNA processing in this system using state-of-the-art ultrahigh-throughput sequencing methods (so-called RNAseq). We thereby hope to systematically catalog the aberrant changes in SMA muscle cells at different stages of differentiation and innervation. Hopefully, we will be able to identify new disease mechanisms that underlie the muscle wasting in SMA and thereby also provide novel potential therapeutic approaches for this disease.

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